

EXHIBIT 1

Application for Reissue of
U.S. Patent No. 4,775,624
of

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for

VECTORS AND COMPOUNDS
FOR EXPRESSION OF HUMAN
PROTEIN C

Nascent protein—the polypeptide produced upon translation of a mRNA transcript; prior to any post-translational modifications.

pA—a DNA sequence encoding a polyadenylation signal.

Promoter—a DNA sequence that directs transcription of DNA into RNA.

Protein C activity—any property of human protein C responsible for biological function or antihuman protein C antibody-binding activity.

Recombinant DNA Cloning Vector—any autonomously replicating agent, including, but not limited to, plasmids and phages, comprising a DNA molecule to which one or more additional DNA segments can be or have been added.

Recombinant DNA Expression Vector—any recombinant DNA cloning vector into which a promoter has been incorporated.

Replicon—A DNA sequence that controls and allows for autonomous replication of a plasmid or other vector.

Restriction Fragment—any linear DNA sequence generated by the action of one or more restriction endonuclease enzymes.

RSV LTR—a DNA segment comprising the promoter activity of the Rous Sarcoma virus long terminal repeat.

Sensitive Host Cell—a host cell grow in the presence of a given antibiotic or other toxic compound without a DNA segment that confers resistance thereto.

Structural Gene—any DNA sequence that encodes a functional polypeptide, inclusive of translational start and stop signals.

TcR—the tetracycline-resistant phenotype or gene conferring same.

Transformation—the introduction of DNA into a recipient host cell that changes the genotype of the recipient cell.

Transformant—a recipient host cell that has undergone transformation.

Translational Activating Sequence—any DNA sequence, inclusive of that encoding a ribosome binding site and translational start codon, such as 5'-ATG-3', that provides for the translation of a mRNA transcript into a peptide or polypeptide.

Zymogen—an enzymatically inactive precursor of a proteolytic enzyme.

DETAILED DESCRIPTION OF THE INVENTION

The present invention comprises novel DNA compounds encoding human protein C activity. Depicting only the coding strand of the molecule for convenience, the novel compounds comprise the sequence:

5'-R ₁ N—R _M —GCC													
AGC	CTG	GAG	CGG	GAG	TGC	TTC	CTG	GAG	GAG	CTC	CGT	CAC	AGC
GAG	GCC	AAG	GAA	ATT	TTC	CAA	AAT	GTG	GAT	GAC	GAC	TTC	GAG
TTC	TGG	TCC	AAG	CAC	GTC	GAC	GGT	GAC	CAG	TGC	TTG	GTC	TTG
CCC	TTG	GAG	CAC	CCG	TGC	GCC	AGC	CTG	TGC	TGC	GGG	CAC	GGC
ACG	TGC	ATC	GAC	GGC	ATC	GGC	AGC	TTC	AGC	TGC	GAC	TGC	CGC
AGC	GGC	TGG	GAG	GGC	CGC	TTC	TGC	CAG	CGC	GAG	GTG	AGC	TTC
CTC	AAT	TGC	CTG	GAC	AAC	GGC	GGC	TGC	ACG	CAT	TAC	TGC	
CTA	GAG	GAG	GTG	GGC	TGG	CGG	CGC	TGT	AGC	TGT	GCG	OCT	GGC
TAC	AAG	CTG	GGG	GAC	GAC	CTC	CTG	CAG	TGT	CAC	CCC	GCA	GTG
AAG	TTC	CCT	TGT	GGG	AGG	CCC	TGG	AAG	CGG	ATG	GAG	AAG	AAG
CGC	AGT	CAC	CTG	AAA	CGA	GAC	ACA	GAA	GAC	CAA	GAA	GAC	CAA
GTA	GAT	CCG	CGG	CTC	ATT	GAT	GGG	AAG	ATG	ACC	AGG	CGG	GGA
GAC	AGC	CCC	TGG	CAG	GTG	GTC	CTG	CTG	GAC	TCA	AAG	AAG	AAG
CTG	GCC	TGC	GGG	GCA	GTG	CTC	ATC	CAC	CCC	TCC	TGG	GTG	CTG

-continued

ACA	GCG	GCC	CAC	TGC	ATG	GAT	GAG	TCC	AAG	AAG	CTC	CTT	GTC
AGG	CTT	GGA	GAG	TAT	GAC	CTG	CGG	CGC	TGG	GAG	AAG	TGG	GAG
CTG	GAC	CTG	GAC	ATC	AAG	GAG	GTC	TTC	GTC	CAC	CCC	AAC	TAC
AGC	AAG	AGC	ACC	ACC	GAC	AAT	GAC	ATC	GCA	CTG	CTG	CAC	CTG
GCC	CAG	CCC	GCC	ACC	CTC	TCG	CAG	ACC	ATA	GTG	CCC	ATC	TGC
CTC	CCG	GAC	AGC	GGC	CTT	GCA	GAG	CGC	GAG	CTC	AAT	CAG	GCC
GGC	CAG	GAG	ACC	CTC	GTG	ACG	GGC	TGG	GGC	TAC	CAC	AGC	AGC
CGA	GAG	AAG	GAG	GCC	AAG	AGA	AAC	CGC	ACC	TTC	GTC	CTC	AAC
TTC	ATC	AAG	ATT	CCC	GTG	GTC	CCG	CAC	AAT	GAG	TGC	AGC	GAG
GTC	ATG	AGC	AAC	ATG	GTG	TCT	GAG	AAC	ATG	CTG	TGT	GCG	GGC
ATC	CTC	GGG	GAC	CGG	CAG	GAT	GCC	TGC	GAG	GGG	GAC	AGT	GGG
GGG	CCC	ATG	GTC	GCC	TCC	TTC	CAC	GGC	ACC	TGG	TTC	CTG	GTG
GGC	CTG	GTG	AGC	TGG	GGT	GAG	GGC	TGT	GGG	CTC	CTT	CAC	AAC
TAC	GGC	GTT	TAC	ACC	AAA	GTC	AGC	CGC	TAC	CTC	GAC	TGG	ATC
CAT	GGG	CAC	ATC	AGA	GAC	AAG	GAA	GCC	CCC	CAG	AAG	AGC	TGG
GCA	CCT	TAG-3'											

wherein

A is deoxyadenyl,

G is deoxyguanyl,

C is deoxycytidyl,

T is thymidyl,

R is 5'-GCC CAC CAG GTG CTG CGG ATC

CGC, AAA CGT-3' or 5'-CAC CAG GTG CTG

CGG ATC CGC AAA CGT-3'

R¹ is

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT-3'	
or 5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC	GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT	CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT	GCC-3'

M is 0 or 1, and

N is 0 or 1,

provided that when M is 0, N must necessarily also be 0;
and that when